Memoranda
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Memoranda are statements concerning the conclusions or recommendations of certain WHO scientific meetings; they are signed by the participants in the meeting.

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Acquired immunodeficiency syndrome — an assessment of the present situation in the world: Memorandum from a WHO Meeting*

A consultative meeting was convened by the World Health Organization in Geneva on 22-25 November 1983 to assess the present situation of AIDS (the acquired immunodeficiency syndrome) in the world and to encourage collaboration between the different nations affected by this disease. AIDS was first reported in the USA in 1981, but probably existed there as early as 1978. Soon after its recognition in the USA, similar cases were identified in other areas of the world. In most western European countries and Canada, the epidemiological pattern is very similar to that in the United States, the majority of cases being in homosexual men. In other areas such as equatorial Africa and the Caribbean, the pattern seems to be different with no identifiable risk factors for the majority of cases.

The disease is manifested by opportunistic infections and/or selected malignancies, with apparent differences in the clinical presentation between the cases in North America and Europe, on the one hand, and those in the tropics. To date there is no treatment that has significantly improved the underlying cellular immune deficiency, and the mortality is very high. The etiology of AIDS is unknown, but the epidemiological pattern is most consistent with its being caused by a transmissible agent; retroviruses come on top of the list of candidate agents. Despite the unknown etiology and the lack of laboratory diagnostic tests, sufficient information is available to permit health authorities to make recommendations that may reduce appreciably the incidence of the disease.

AIDS is an important health problem in a number of countries and has international implications. Collaborative laboratory, epidemiological and clinical research between countries is needed to accelerate control efforts. In the meantime, WHO will coordinate exchange of information among countries.

The acquired immunodeficiency syndrome (AIDS), a clinical entity that includes fatal opportunistic infections and rare malignancies, was first reported in the USA in 1981, though retrospective studies indicate that the first cases occurred there as early as 1978. Soon after these first reports, similar cases began to be reported from other areas of the world. As in the United States, retrospective studies indicated that AIDS in equatorial Africa and the Caribbean region may also have occurred during the late 1970s. In some of these areas, such as in most western European countries and Canada, the epidemiological pattern is very similar to that in the United States, the majority of cases being in homosexual men. In other areas, such as equatorial Africa and the Caribbean, the pattern seems to be different, with no identifiable risk factor for the majority of cases.

This memorandum reviews current information on AIDS and gives conclusions and recommendations concerning epidemiology and surveillance, etiology, clinical diagnosis and management, and prevention and control.

* This Memorandum was drafted by the signatories listed on pages 427-428 during a consultative meeting convened by WHO in Geneva on 22-25 November 1983. Requests for reprints should be addressed to the Director, Division of Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland. A French translation of this Memorandum will appear in a later issue of the *Bulletin*.

EPIDEMIOLOGY AND SURVEILLANCE

The epidemiological pattern of AIDS differs according to geographical area and is described below separately for each area.

North America

United States of America. There is no specific diagnostic test for AIDS. For surveillance purposes the Centers for Disease Control (CDC) adopted criteria in 1981 for defining AIDS. These criteria included reliably diagnosed marker conditions considered indicative of severe underlying immunodeficiency with no identifiable cause (see Annex 1). This definition has been useful for monitoring trends and detecting disease patterns, but it underestimates the extent of the problem. Clinicians have recognized that a variety of chronic but nonspecific symptoms and physical findings may also be related to the syndrome.

AIDS is a notifiable condition in most States and diagnosed cases have increased considerably since 1981 (Fig. 1). However, retrospective studies have revealed a small number of cases diagnosed as early as 1978. Cases diagnosed in 1983 are underestimated in Fig. 1 because of the lag between date of diagnosis and date of report for many cases. Nearly 75% of all the cases have been reported in the past 12 months (that is, since November 1982). Over 40% of the cases are known to have been fatal. Fewer than 20% of patients have survived 2 years after AIDS was diagnosed.

Over 70% of reported cases in the United States have been in homosexual or bisexual men (Table 1). The 326 patients listed as "other" include 26 (1%) who were reported to be sexual contacts of persons in populations with an increased incidence of AIDS, 19

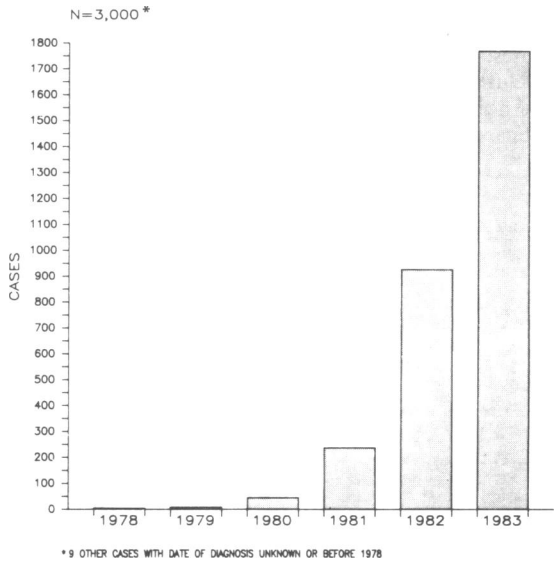

Fig. 1. Cases of AIDS in the United States, by year of diagnosis, 1978–1983, reported by 19 December 1983.

(0.7%) with haemophilia and no other known risk factor, 33 (1%) who had received blood transfusions within 5 years before diagnosis, 131 (4.8%) who were persons born in Haiti but were not identified as being in a risk group, and 12 (0.4%) with Kaposi's sarcoma and a normal immunological status. It is likely that most of these sarcoma patients represent "background" cases of classic Kaposi's sarcoma rather than AIDS. Of the remaining 105 (3.6%), more than half died before an adequate risk factor history could be obtained.

AIDS has primarily affected young adults, 90% of the patients being in the 20–49-year age group.

Table 1. AIDS cases in the United States, as reported by CDC by 5 December 1983, by patients' characteristics and sex

Patients' characteristics[a]	Males		Females		Total	
	No. of cases	Percentage of all males	No. of cases	Percentage of all females	No. of cases	Percentage of total
Homosexual or bisexual	2052	76.6	0	0.0	2052	71.5
Intravenous drug user	387	14.5	103	54.5	490	17.1
Other	240	9.0	86	45.5	326	11.4
Total	2679	100.0	189	100.0	2868	100.0

[a] Patients' characteristics are ordered hierarchically; cases with multiple characteristics are tabulated only in the group listed first (homosexual or bisexual).

Although cases have been reported from 42 out of 50 States, the syndrome has been concentrated in only five urban areas (Table 2).

Additionally, 35 cases of "paediatric AIDS" have been reported to CDC. Although the difficulty in ruling out other causes of immunodeficiency in infants has made the acceptance of this condition controversial, reported cases are increasing. Approximately two-thirds of paediatric patients were born into families of persons in AIDS high-risk groups and more than half of the remaining third have a history of having received blood transfusions.

Table 2. AIDS cases per million population,[a] by standard metropolitan statistical area (SMSA) of residence, reported from 1 June 1981 to 5 December 1983, in the United States

SMSA of residence	No. of cases	Percentage of total	Cases per million population
New York, NY	1208	42.1	132.5
San Francisco, CA	344	12.0	105.8
Miami, FL	123	4.3	75.7
Newark, NJ	78	2.7	39.7
Los Angeles, CA	227	7.9	30.4
Elsewhere	888	31.0	4.4
Total (for USA)	2868	100.0	12.7

[a] From the 1980 census.

Canada. As of 15 November 1983, 50 cases have been reported from Canada, 22 (44%) of them from Montreal. The epidemiological pattern is similar to that in the United States.

Europe

AIDS has been increasingly reported in many countries in Europe (Table 3) where the risk factors and demographic characteristics resemble those in the United States, with over 70% of cases occurring in homosexual men. Fewer than 2% of cases have occurred in heterosexual abusers of intravenous drugs and 4% in persons with haemophilia. It is noteworthy that 59 (22%) out of 266 cases reported in Europe have been among persons born in Africa (including Burundi, Cameroon, Chad, Congo, Gabon, Mali, Rwanda, and Zaire); 37% of the African patients

Table 3. Cases of AIDS reported to the WHO Regional Office for Europe by 20 October 1983[a]

Country	Year of diagnosis						Total
	Before 1979	1979	1980	1981	1982	1983	
Austria						7	7
Belgium			2	4	8	24	38
Denmark			1	2	4	6	13
Finland						2	2
France	6	1	5	5	30	47	94
Germany, Federal Republic of	1	1			7	33	42
Ireland						2	2
Italy	1				2		3
Netherlands					3	9	12
Norway						2	2
Spain				1	1	4	6
Sweden					1	3	4
Switzerland			2	3	5	7	17
United Kingdom				2	5	17	24
Total	8	2	10	17	66	163	266

[a] German Democratic Republic, Greece, Hungary, Luxembourg, Poland, USSR, and Yugoslavia reported no cases. Two suspected cases in Czechoslovakia did not prove to be AIDS. No information was received from other countries.

were women. No specific risk factors could be identified for the majority of these patients.

The Caribbean

In retrospect, sporadic cases of AIDS were diagnosed in young adults in Haiti as early as 1979. However, most of the November 1983 total of 202 cases were reported since the beginning of 1982; 82% of the patients were in the 20–40-year age group, 85% were men, and over 80% were from the Port-au-Prince metropolitan area. In a special study of a subgroup of these patients, potential risk factors (bisexual activity, receipt of blood transfusions) were identified for 12% of the men and 22% of the women with AIDS. All educational and socioeconomic levels have been affected.

In addition to risk factors previously recognized for other groups, the role of other possible factors such as heterosexual transmission is being examined. Exposure to unsterilized needles unassociated with drug abuse is of potential importance. There has been no evidence of spread through water, air, food, or ordinary social contact.

Equatorial Africa

Because of recent reports documenting an increase in cryptococcal meningitis in Zaire and because Zairian patients with AIDS have recently been reported in Europe, a special study on AIDS was undertaken in Kinshasa. The clinical criteria for suspected AIDS cases included one or more of the following: diarrhoea of at least 2 months' duration with weight loss of 10% or more of the body weight, unexplained recurrent fever, pneumonia of unknown etiology refractory to standard therapy, cryptococcal meningitis, Kaposi's sarcoma, and presence of other serious opportunistic infections (e.g., oro-oesophageal candidiasis). T-cell subsets were determined on persons clinically suspected of having AIDS and demonstrating skin test anergy with either multiple antigens or tuberculin. Persons meeting the clinical criteria, having skin test anergy, and having an absolute number of T-helper cells of < 400 and a T-helper/suppressor ratio of < 0.6 were considered as AIDS patients.

In October and November 1983, 49 cases of AIDS were diagnosed in two large hospitals in Kinshasa, 41% of these being in women. No definite risk factors have been identified. The mean ages of male and female AIDS patients were 42 and 30 years, respectively; 21% of the men and 90% of the women were unmarried. All social and economic groups and geographical regions were represented; over 80% of the AIDS patients were residents of Kinshasa.

Other areas

Besides the cases in the United States, Canada, and Haiti, there were 44 cases of AIDS in the Americas reported to the Pan American Health Organization as of 12 September 1983. Of these 44 cases, 12 were reported from Argentina, 22 from Brazil, 4 from Mexico, 2 from Jamaica, 2 from Uruguay, 1 from Suriname, and 1 from Trinidad and Tobago.

Five AIDS cases in homosexual men have been reported from Australia. Two suspected cases have been reported from Japan.

CLINICAL DIAGNOSIS AND MANAGEMENT

General considerations

AIDS results from cellular immune deficiency and is manifested by opportunistic infections and/or selected malignancies. Clinical diagnosis of fully expressed AIDS would ordinarily satisfy the following criteria: (1) a reliable diagnosis of opportunistic infection and/or malignancy (Annex 1), the latter including Kaposi's sarcoma, B cell lymphoma, and possibly other tumours; (2) evidence of cellular immune deficiency (characteristically, AIDS patients show skin test anergy, persistent reduction of T-helper cells, decreased ratio of T-helper to T-suppressor cells, impaired proliferative response to mitogens and antigens, reduced cellular cytotoxicity, and increased serum immunoglobulins); (3) failure to identify a cause for the cellular immune deficiency, such as primary immunodeficiency syndromes, corticosteroid therapy, chemotherapy or radiotherapy, or pre-existing diseases such as malignancies or severe protein-energy malnutrition.

Since the symptoms alone are not specific for AIDS, a careful history concentrating upon epidemiological risk factors may be helpful in differential diagnosis and management.

Clinical features and management

Opportunistic infections. A striking feature of the AIDS syndrome is the wide spectrum and frequency of infections (Annex 1). The organisms causing the disease are life-threatening pathogens seldom seen in normal hosts. The illness in AIDS patients may begin with insidious signs and symptoms, and the process may be more diffuse than when the same conditions are seen in other immunocompromised patients. These findings are consistent with a limited immune response by the patient and inability to contain the infection.

Four patterns of disease occur in AIDS patients. The "pulmonary pattern" consists of dyspnoea,

hypoxaemia, chest pain, and diffuse pulmonary infiltrates on chest X-ray. The most prevalent fatal infection in North America and Europe has been *Pneumocystis carinii* pneumonia, and there is a high recurrence rate after stopping therapy. In addition to *Pneumocystis carinii*, *Legionella pneumophila* and cytomegalovirus (CMV) infections produce a similar pulmonary picture.

The "central nervous system pattern" is seen in about 30% of AIDS cases and occurs in four major forms: (1) infections including *Toxoplasma gondii* abscesses, cryptococcal meningitis, progressive multifocal leukoencephalopathy, *Mycobacterium avium intracellulare* infection, and subacute encephalitis possibly attributable to cytomegalovirus infection; (2) tumours such as cerebral lymphoma; (3) vascular complications including non-bacterial thrombotic endocarditis and cerebral haemorrhage associated with thrombocytopenia; (4) central nervous system problems with focal brain lesions and self-limiting aseptic meningitis.

The "gastrointestinal pattern" with diarrhoea and weight loss in AIDS cases has been associated with enteric infections with *Cryptosporidium* and other organisms. In many cases the cause of the weight loss and diarrhoea remains unclear.

The pattern of "fever of unknown origin" with weight loss, malaise, and weakness is also seen. *Mycobacterium avium intracellulare* infections have been demonstrated in bone marrow, lymph nodes, or liver biopsy specimens from some of these individuals.

Most patients who recover from a given infection develop subsequent opportunistic infections either as a relapse or as a result of infection with a new agent. Many patients continue to have a wasting syndrome and experience infections such as oral thrush.

Malignancies. Over 30% of the patients with AIDS described in North America and Europe have Kaposi's sarcoma. The disease is histologically indistinguishable from previously recognized Kaposi's sarcoma both in the United States and in Africa. However, a number of clinical features differ. For example, traditional Kaposi's sarcoma is usually limited to the extremities, but in AIDS it is often generalized, with lymph node, mucous membrane, and visceral involvement. Patients with traditional Kaposi's sarcoma usually have an indolent course and respond to radiation or chemotherapy, but in AIDS patients it is more aggressive and the response to chemotherapy has been variable. Furthermore, many clinicians have avoided using chemotherapy to avoid further compromising the patients' immunological status. AIDS patients with Kaposi's sarcoma usually have life-threatening opportunistic infections.

An excess incidence of undifferentiated non-Hodgkin's lymphoma and of primary central nervous system lymphoma has been observed in populations with a higher incidence of AIDS.

Other clinical aspects. Depression and a feeling of isolation are common among AIDS patients. There is often anxiety about transmitting AIDS to intimate contacts. Health care workers who display fear of patients with AIDS contribute further to the patients' feelings of depression and isolation.

Immunological features. Skin-test anergy is common in patients with AIDS, and much evidence indicates that the immunopathology of AIDS is largely within the cellular immune system. One of the two major subpopulations of T-cells,[a] the T-helper cells, is characteristically reduced in AIDS patients. Furthermore, the ratio of T-helper to T-suppressor cells is usually reduced as a consequence of the T-helper cell reductions and in some T-suppressor cell increases. T-cell functions, such as proliferative responses to mitogens and antigens, and cytotoxic functions are characteristically reduced in AIDS patients. B cells are often activated as evidenced by elevated serum levels of IgG and IgA and increased B cell regions in the enlarged lymph node.

Treatment. To date, no therapy has resulted in significant improvement of the underlying cellular immune deficiency. The present treatment of AIDS involves specific therapies for infectious diseases and cancers as well as supportive care.

Trimethoprim-sulfamethoxazole (TMP-SMZ) is the drug of choice for *Pneumocystis carinii* pneumonia. Many patients with AIDS, however, have toxic allergic reactions to TMP-SMZ, including a morbilliform eruption or profound leukopenia. Such patients with *Pneumocystis carinii* pneumonia or those who fail to respond to TMP-SMZ treatment are treated with pentamidine-isetionate. The prognosis for AIDS patients with Kaposi's sarcoma (without opportunistic infections) is generally better than for other AIDS patients if they do not develop other opportunistic infections.

Clinical presentations in tropical countries. Initial observations about the clinical presentations of AIDS in Haiti and Zaire indicate some differences from AIDS in North America and Europe. Maculopapular rashes and gastrointestinal problems including severe, persistent diarrhoea and oral and oesophageal candidiasis have been recognized more frequently in

[a] T lymphoid cells can be divided into two major subpopulations on the basis of distinctive surface antigens recognized by monoclonal antibodies. Antigens T4 and Leu 3 are characteristic of the numerically larger subpopulations and T8 and Leu 2 of the numerically smaller subpopulation. T-helper induced functions are associated with the former group, and many T-suppressor/cytotoxic functions are found in the latter group. These correlations are not absolute, however. In clinical publications the T-helper and T-suppressor terms are commonly used to describe the two distinctive subsets.

patients from Haiti and Zaire. Localized and disseminated tuberculosis is also more common and may respond poorly to therapy. *Pneumocystis carinii* pneumonia and Kaposi's sarcoma affect a smaller proportion of patients from Zaire and Haiti with AIDS. Toxoplasmosis of the central nervous system has been diagnosed with greater frequency among Haitians with AIDS, and cryptococcal meningitis more frequently among patients from Zaire. Persistent lymphopenia, oral thrush, or cutaneous anergy indicate the need for further evaluation of patients with unexplained symptoms. Patients should be referred to centres where further diagnosis and therapy for AIDS-associated conditions are available.

AIDS-related symptom complex. Persons in populations with an increased incidence of AIDS may exhibit one or more of the following clinical features: lymphadenopathy, fatigue/malaise, anorexia, weight loss greater than 10% of body weight, fever, night sweats, unremitting diarrhoea, thrombocytopenia, or milder opportunistic infections. Laboratory evidence of cellular immune changes is found in many of these patients. Though such symptoms are often considered AIDS-related, they may represent a milder form of the illness since the follow-up of selected groups of homosexual men with this symptom complex indicate that fewer than 10% manifest the life-threatening form of AIDS within 1 year.

ETIOLOGY

The etiology of AIDS is unknown, but the epidemiological pattern is most consistent with its being caused by a transmissible agent. Transmission of the presumed agent of AIDS appears to occur by sexual contact, by blood sharing (either by therapeutic blood or blood products or by shared needles used for illicit drugs), or during the birth process (possibly intrauterine).

Although there are other etiological possibilities, either alone or as cofactors, the most likely cause of AIDS is a virus. Support for this is based on observations that (1) the disease distribution is similar to hepatitis B in many industrial countries, (2) the pathophysiological characteristics of the disease resemble those due to some animal viruses (e.g., feline leukaemia virus), (3) AIDS occurs in recipients of filter-sterilized blood coagulation factors, so that the putative agent must be capable of passing through such filters, (4) epidemiological findings are consistent with person-to-person spread, and (5) all attempts to link bacteria, mycoplasma, fungi, and similar agents to AIDS have been unsuccessful to date.

The search for a candidate agent has involved many laboratories and most of the known microbiological and biochemical techniques. Transmission experiments with laboratory animals and non-human primates are in progress.

Serological testing of blood from AIDS patients has revealed a high prevalence of infection with cytomegalovirus, Epstein-Barr virus, alpha herpesviruses 1 and 2, hepatitis B virus, and heptatitis A virus. However, tests on serum samples from AIDS patients and well-matched controls have provided no convincing evidence that these agents have an etiological role.

Conventional isolation attempts have also yielded evidence of infection with herpesviruses and adenoviruses. The most common isolates have been cytomegalovirus and Epstein-Barr virus. The former has been suggested as a candidate agent for AIDS because of its high prevalence in the populations at risk for AIDS and because CMV-associated syndromes have been described as having clinical and laboratory evidence of immunosuppression, such as temporary inversion of the T-helper/T-suppressor ratio. Adenoviruses have been isolated less frequently, and isolates are of various genotypes and serotypes.

Retroviruses have been considered as candidate agents for AIDS. Certain retroviruses are capable of causing immunosuppressive and neoplastic diseases in animals after long latency periods. Since retroviruses produce chronic viraemia, they could also be transmitted by blood. The best characterized human retrovirus, human T-cell leukaemia virus (HTLV), has tropism for T-cells of the helper-inducer phenotype; these infected phenotypic helper cells have been shown to be functionally incompetent.

Several laboratories in various parts of the world have identified retroviruses in cultures of lymphocytes from patients with AIDS or lymphadenopathy. In addition, HTLV-related nucleic acid sequences have been detected in cultured cells from a few AIDS patients. Antibodies to membrane antigens on the surface of HTLV-infected lymphocytes and to purified virus isolates have been found in patients with AIDS. The prevalence of membrane-associated antibodies in patients with AIDS or in homosexual men with generalized lymphadenopathy has been significantly higher than in controls, though the prevalence in AIDS patients does not exceed 50%.

PREVENTION AND CONTROL

General considerations

Sufficient information is available now to permit health authorities to make certain recommendations that may decrease the incidence of AIDS among the

groups that are at highest risk of acquiring the syndrome. For example, epidemiological data in North America and Europe indicate that the majority of AIDS cases occur in homosexual men, those with multiple sexual partners being at highest risk. These findings permit public health authorities in North America and Europe to work together with representatives of homosexual groups to formulate and distribute recommendations to lower the risk of contracting AIDS for homosexual men.

Spouses of AIDS patients have also been shown to be at an increased risk of acquiring the syndrome. Whether persons with multiple heterosexual sex partners are at greater risk of acquiring AIDS is unknown; the low incidence in North America and Europe suggests that the risk is probably considerably less than that for homosexual men.

Although the mode of transmission in tropical countries is not clear, injections with unsterile needles and syringes may play a role since sharing of contaminated needles has been perceived as the risk factor among drug users in North America. Local health authorities can make it clear that improper sterilization of needles and syringes for medical purposes theoretically increases the risk for transmitting AIDS, as well as other infections.

Education of the public and medical professionals

There have been many misconceptions about AIDS resulting from transmittal of inaccurate or incomplete information, often resulting in the stigmatization of groups afflicted with AIDS. National advisory boards or committees have effectively combated these and other problems by providing factual, up-to-date information to the communications media and by making recommendations to specific groups.

Health care workers and allied professionals

There has been no firm evidence of occupationally related transmission of AIDS to health care workers, although more than 3000 patients have been taken care of in many hospitals and clinics throughout the world. Of the more than 2600 AIDS patients in the United States, 4 were reported to be health care personnel not known to belong to groups at increased risk for AIDS. None of these 4 patients had had direct known exposure to AIDS patients in the course of duty. Despite these findings, caution should be exercised by those involved in direct patient care or in work with clinical or laboratory specimens.

In industrial countries the epidemiological pattern of AIDS resembles the disease distribution and mode of spread of hepatitis B virus. Therefore, the precautions when taking care of AIDS patients and when handling specimens from these patients should be similar to the recommended precautions when dealing with hepatitis B patients, whose blood or body fluids that might have been contaminated with blood are considered infective. The current concern with AIDS serves as a reminder that laboratory workers must always employ good laboratory practice when handling blood and tissue specimens.

In the United States, guidelines have been issued by the Centers for Disease Control for clinical and laboratory staff, dental care personnel, persons performing necropsies or providing mortician services, and persons handling or taking care of experimental animals inoculated with potentially infectious materials (Annex 2).

Blood and blood products

AIDS cases have occurred both in haemophiliacs receiving clotting factor concentrates and in recipients of blood and blood component transfusions who do not have other apparent risk factors. Approaches to reducing the possibility of spreading AIDS by blood and blood products include (1) educating the general public and donor groups, (2) excluding donors who belong to established risk groups, (3) avoiding non-essential use of blood and blood products, and (4) preparing and using blood and blood products in such a way as to reduce the risk of transmitting AIDS. The following recommendations are made in the absence of a specific, reliable laboratory test for AIDS. Should such a test become available, these recommendations will need to be reviewed.

(*a*) *Donor education and selection.* Some countries have recommended that persons with AIDS and members of populations with an increased incidence of AIDS should voluntarily refrain from donating blood or plasma. Good communication with the donor population is essential to achieve voluntary self-exclusion by risk groups; this requires continuous effort by blood and plasma-collecting organizations. Such self-exclusion is likely to be more effective with volunteer (unpaid) donors. Voluntary unremunerated blood donation was urged by the World Health Assembly in 1975 (resolution WHA 28.72). It should also be known that there is no risk of acquiring AIDS by donating blood or plasma under conditions where sterile collection equipment is used.

Donors selected because they have a high titre of antibodies to hepatitis B virus or cytomegalovirus may be more likely to be members of AIDS risk groups in some countries. This possibility should be considered in the preparation and use of blood products from such individuals. In addition, in situations where human blood or blood components are used to produce hyperimmune materials, precautions must be taken to ensure the safety of the immunized donor.

(*b*) *Donor screening using non-specific tests to recognize high-risk groups.* Even in the absence of a specific screening test, laboratory procedures may theoretically help to identify individuals who are at risk of AIDS and who should not be accepted as donors. Such tests, which have been proposed by several investigators, would tend to identify phenomena indirectly related to particular risk groups. Since these tests are not direct measures of AIDS or of the susceptibility to AIDS, a certain number of individuals not belonging to a risk group would be excluded from donating blood. This number may vary considerably in different parts of the world, depending upon the characteristics of the risk groups. Thus, the specificity and sensitivity of any such test(s) for this purpose must be evaluated in the environment in which it is to be applied, taking into consideration the potential effectiveness of the test as well as the impact on the blood supply and the potential alienation of donors.

(*c*) *Record-keeping.* Accurate and confidential records are required in blood and plasma donation centres in order to facilitate epidemiological studies correlating donor and recipient data.

(*d*) *Sample collection.* The development of selected serum repositories in blood banks is required for prospective studies.

(*e*) *Plasma processing.* Current evidence suggests that immunoglobulin and albumin prepared by generally accepted methods have not been implicated in AIDS and are considered safe. Coagulation factor concentrates, however, have been implicated in cases of AIDS. Although additional inactivation methods have recently been developed, it will not be possible fully to establish their effectiveness until the causative agent of AIDS is discovered.

There are two approaches to minimizing the risk associated with processed plasma fractions: (1) reduce the number of donors contributing to the products a patient receives, and (2) employ processing technology aimed at reducing contamination risks. Plasma fractions may be produced from single donor material or from pools obtained from up to 20 000 donors. Since small-pool products expose patients to smaller numbers of donors than large-pool concentrates, individual patients regularly treated with small-pool products have a lower theoretical risk of exposure.

Another approach to reducing the risk of AIDS from plasma fractions is to use specified donor material for a given recipient. An extension of that concept is to use a specified batch of material from a pool of a given size, thus reducing the number of donor exposures by the patient. Use of the specified donor-recipient approach for persons with newly diagnosed haemophilia requiring only infrequent therapy should be explored.

(*f*) *Human hepatitis B virus vaccine.* Requirements for hepatitis B vaccines, including aspects of safety, have been formulated and have been reviewed by WHO.[b] Preparations that meet these requirements are considered safe.

CONCLUSIONS AND RECOMMENDATIONS

AIDS is an important health problem in several countries of the world and has international implications, the number of cases increasing steadily since it was first reported in the United States in 1981. The disease is associated with homosexual men with multiple partners, needle-sharing among abusers of intravenous drugs, use of pooled plasma products by persons with haemophilia, and blood transfusions. AIDS has only recently been recognized in tropical countries, and little is known about risk factors or transmission. AIDS is not known to spread through non-intimate social contact. In the absence of a specific diagnostic test for AIDS, a clinical case-definition has served well for surveillance purposes for the past few years. Using this basic definition, surveillance should be initiated throughout the world to monitor trends and to detect the first occurrence of cases in populations not now known to have an increased incidence of AIDS.

Collaborative research between and within countries is needed to broaden the understanding of AIDS and to accelerate the development of control efforts. Several areas deserve emphasis.

— *Laboratory research* on the etiology of AIDS could be expedited by sharing of scientific information, reagents, specimens, and putative agents; and by collaboration on transmission experiments in animals, including nonhuman primates.

— *Epidemiological research* could benefit greatly from collaborative studies in geographical areas where AIDS has been recognized and where risk factors are poorly understood, studies on the relationship of endemic Kaposi's sarcoma to AIDS, and studies on the use of nonspecific laboratory tests to determine their effectiveness in excluding high-risk persons as well as the impact of such tests on the supply of blood.

— *Clinical research* could be assisted by studies on therapy for both the immunodeficiency condition itself and the various opportunistic infections to

[b] WHO Technical Report Series, No. 658, 1981 (*WHO Expert Committee on Biological Standardization*: thirty-first report), Annex 4, pp. 131–156. An updated version is to be discussed at a meeting in June 1984.

reduce the high case-fatality rate, studies on the disease spectrum of AIDS, especially in tropical countries, and studies on the relationship of AIDS and other immunodeficiencies to tuberculosis, leprosy, sexually transmitted diseases, and malnutrition.

The occurrence of AIDS places severe burdens on medical staff and facilities, whether in industrial or non-industrial communities. Referral to centralized facilities for the diagnosis and care of patients with AIDS is to be encouraged in areas with limited medical and laboratory facilities. In such areas, physicians and other health care personnel should be informed regarding the clinical and laboratory information necessary for diagnosis and management, the precautions for personnel caring for patients or handling laboratory specimens, and the social and behavioural concerns associated with the syndrome.

Sufficient information is available at the present time to permit health authorities to make recommendations which may decrease the incidence of AIDS among certain risk groups. However, the impact of these measures will initially be difficult to evaluate since the average period between exposure and diagnosis of AIDS may exceed 2 years. Measures which may be instituted now include:

— training medical and technical personnel to use only adequately sterilized injection equipment for medical purposes.

— persuading individuals with AIDS and persons in groups with an increased incidence of AIDS to refrain from donating blood and plasma. Blood- and plasma-collecting organizations should provide relevant information about AIDS to promote this voluntary self-exclusion policy.

— providing information to homosexual men to prevent the sexual transmission of AIDS in this group.

— informing persons with haemophilia and their physicians of the potential health hazards of factor VIII or IX products, including the risks related to AIDS.

— considering the use of autotransfusion with frozen or conventionally stored blood for suitable patients.

Because of WHO's special position in the international health field, it can provide a unique resource in developing an understanding of AIDS and in planning strategies for eventual control. The participants at the meeting therefore recommend the following:

(1) The criteria for AIDS diagnosis and surveillance described in Annex 1 should be adopted for epidemiological use in all industrial countries. An adaptation of these criteria may be necessary for surveillance in countries without extensive laboratory or other specialized facilities, but to ensure consistency in case definition and allow assistance where required, WHO should be notified by all countries proposing to use any modified criteria. Consistent use of a suitable definition is essential for comparing data from different countries.

(2) Collaborative research on AIDS between countries should be encouraged and supported.

(3) The safety precautions recommended for personnel taking care of patients with AIDS or handling laboratory specimens should be widely publicized.

(4) The specifications for blood and blood products should be reviewed regularly and modifications, where appropriate in the light of additional information on AIDS transmission, should be recommended.

(5) The recently designated WHO centre for AIDS information exchange in Europe (in Paris) should be requested to coordinate the exchange of information between regions of the world, particularly between developing and industrial countries of the world. AIDS surveillance information should be made available on a regular basis through publications.

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Annex 1

CDC criteria for AIDS diagnosis and surveillance

I. *Diseases at least moderately predictive of cellular immunodeficiency in the United States.*

A. Malignancies

1. Kaposi's sarcoma in persons less than 60 years of age (based on histopathology).
2. Lymphoma limited to the brain (based on histopathology).

B. Infections

1. *Protozoal and helminthic infections*

   (*a*) *Pneumocystis carinii* pneumonia (based on histology or on microscopy of a "touch" preparation (touching the glass slide with suspected infected material) or bronchial washings).

   (*b*) Toxoplasmosis, causing pneumonia or CNS infection (based on histology or microscopy of a "touch" preparation).

   (*c*) Cryptosporidiosis (intestinal) causing diarrhoea for over one month (based on histology or stool microscopy).

   (*d*) Strongyloidosis, causing pneumonia, CNS infection, or disseminated infection (based on histology).

2. *Fungal infections*

   (*a*) Candidiasis, causing oesophagitis (based on histology, microscopy of a "wet" preparation from the oesophagus, or endoscopic findings of plaques on an erythematous mucosal base).

   (*b*) Cryptococcosis, causing pulmonary, CNS, or disseminated infection (based on culture, antigen detection, histology, or India ink preparation of CSF).

3. *Bacterial infections*

   (*a*) "Atypical" mycobacteriosis (species other than *Mycobacterium tuberculosis* or *M. leprae*), causing disseminated infection (based on culture).

4. *Viral infections*

   (*a*) Cytomegalovirus, causing pulmonary, gastrointestinal tract, or CNS infection (based on histology).

   (*b*) Alpha herpesvirus 1 or 2, causing chronic mucocutaneous infection (with ulcers persisting more than one month) or pulmonary, gastrointestinal tract, or disseminated infection (based on culture, histology, or cytology).

   (*c*) Progressive multifocal leukoencephalopathy (presumed to be caused by papovavirus) (based on histology).

II. *Exclusion criteria*

A. History of recent immunosuppressive therapy before the onset of illness, *or*

B. Presence of another pre-existing illness associated with immunosuppression (e.g., congenital immunodeficiency, lymphoreticular malignancy, severe protein-energy malnutrition)

Annex 2

Precautions for health care workers and allied professionals

A. *Clinical staff*

1. Extraordinary care must be taken to avoid accidental wounds from sharp instruments contaminated with potentially infectious material and to avoid contact of open skin lesions with material from AIDS patients.
2. Gloves should be worn when handling blood specimens, blood-soiled items, body fluids, excretions, and secretions, as well as surfaces, materials, and objects exposed to them.
3. Gowns should be worn when clothing may be soiled with body fluids, blood, secretions, or excretions.
4. Hands should be washed after removing gowns and gloves and before leaving the rooms of known or suspected AIDS patients. Hands should also be washed thoroughly and immediately if they become contaminated with blood.

5. Blood and other specimens should be labelled prominently with a special warning, such as "Blood Precautions" or "AIDS Precautions". If the outside of the specimen container is visibly contaminated with blood, it should be cleaned with a disinfectant (such as a 1:10 dilution of 5.25% sodium hypochlorite household bleach with water). All blood specimens should be placed in a second container, such as an impervious bag, for transport. The container or bag should be examined carefully for leaks or cracks.
6. Blood spills should be cleaned up promptly with a disinfectant solution, such as sodium hypochlorite (see above).
7. Articles soiled with blood should be placed in an impervious bag prominently labelled "AIDS Precautions" or "Blood Precautions" before being sent for reprocessing or disposal. Alternatively, such contaminated items may be placed in plastic bags of a particular colour designated solely for disposal of infectious wastes by the hospital. Disposable items should be incinerated or disposed of in accordance with the hospital's policies for disposal of infectious wastes. Reusable items should be reprocessed in accordance with hospital policies for hepatitis B virus-contaminated items. Lensed instruments should be sterilized after use on AIDS patients.
8. Needles should not be bent after use, but should be promptly placed in a puncture-resistant container used solely for such disposal. Needles should not be reinserted into their original sheaths before being discarded into the container, since this is a common cause of needle injury.
9. Disposable syringes and needles are preferred. Only needle-locking syringes or one-piece needle-syringe units should be used to aspirate fluids from patients, so that the collected fluid can be safely discharged through the needle, if desired. If reusable syringes are employed, they should be decontaminated before reprocessing.
10. A private room is indicated for patients who are too ill to maintain good hygiene, such as those with profuse diarrhoea, faecal incontinence, or altered behaviour secondary to central nervous system infections.

Precautions appropriate for particular infections that occur concurrently in AIDS patients should be added to the above, if needed.

B. *Laboratory staff*

1. Mechanical pipetting devices should be used for the manipulation of all liquids in the laboratory. Mouth pipetting should not be allowed.
2. Needles and syringes should be handled as stipulated in Section A (above).
3. Laboratory coats, gowns, or uniforms should be worn while working with potentially infectious materials and should be discarded appropriately before leaving the laboratory.
4. Gloves should be worn to avoid skin contact with blood, specimens containing blood, blood-soiled items, body fluids, excretions, and secretions, as well as surfaces, materials, and objects exposed to them.
5. All procedures involving, and manipulations of, potentially infectious material should be performed carefully to minimize the creation of droplets and aerosols.
6. Biological safety cabinets (Class I or II) and other primary containment devices (e.g., centrifuge safety cups) are advised whenever procedures are conducted that have a high potential for creating aerosols or infectious droplets. These include centrifuging, blending, sonicating, vigorous mixing, and harvesting infected tissues from animals or embryonated eggs. Fluorescent-activated cell sorters generate droplets that could potentially result in infectious aerosols. Translucent plastic shielding between the droplet-collecting area and the equipment operator should be used to reduce the at present uncertain magnitude of this risk. Primary containment devices are also used in handling materials that might contain concentrated infectious agents or organisms in greater quantities than expected in clinical specimens.
7. Laboratory work surfaces should be decontaminated with a disinfectant, such as sodium hypochlorite solution (see A5 above), following any spill of potentially infectious material and at the completion of work activities.
8. All potentially contaminated materials used in laboratory tests should be decontaminated, preferably by autoclaving, before disposal or reprocessing.
9. All personnel should wash their hands following completion of laboratory activities, and removal of protective clothing, and before leaving the laboratory.

C. *Persons handling experimental animals inoculated with materials from individuals with known or suspected AIDS*

1. Laboratory coats, gowns, or uniforms should be worn by personnel entering rooms housing inoculated animals. Certain nonhuman primates, such as chimpanzees, are prone to throw excreta and to spit at attendants; personnel attending inoculated animals should wear moulded surgical masks and goggles or other equipment sufficient to prevent potentially infective droplets from reaching the mucosal surfaces of their mouths, nares, and eyes. In addition, when handled, other animals may disturb excreta in their bedding. Therefore, the above precautions should be taken when handling them.
2. Personnel should wear gloves for all activities involving direct contact with experimental animals and their bedding and cages. Such manipulations should be performed carefully to minimize the creation of aerosols and droplets.
3. Necropsy of experimental animals should be conducted by personnel wearing gowns and gloves. If procedures generating aerosols are performed, masks and goggles should be worn.
4. Extraordinary care must be taken to avoid accidental sticks or cuts with sharp instruments contaminated with body fluids or tissues of experimental animals inoculated with material from AIDS patients.
5. Animal cages should be decontaminated, preferably by autoclaving, before they are cleaned and washed.
6. Only needle-locking syringes or one-piece needle-syringe units should be used to inject potentially infectious fluids into experimental animals.

D. *Dental care personnel*

1. Personnel should wear gloves, masks, and protective eyewear when performing dental or oral surgical procedures.
2. Instruments used in the mouths of patients should be sterilized after use.

E. *Persons performing necropsies or providing morticians' services*

1. As part of immediate postmortem care, deceased persons should be identified as belonging to one of the above three groups, and a note with identification should remain with the body.
2. The procedures followed before, during, and after the postmortem examination are similar to those for hepatitis B. All personnel involved in performing an autopsy should wear double gloves, masks, protective eyewear, gowns, waterproof aprons, and waterproof shoe coverings. Instruments and surfaces contaminated during the postmortem examination should be handled as potentially infective items.
3. Morticians should evaluate specific procedures used in providing mortuary care and take appropriate precautions to prevent the parenteral or mucous-membrane exposure of personnel to the deceased's body fluids.

Postscript

Acquired immunodeficiency syndrome (AIDS)

For some time, epidemiological evidence has indicated that AIDS is caused by a transmissible infectious agent, most likely a virus. The retroviruses have been considered the leading candidates for two reasons: first, retroviruses may cause, in animals, diseases such as feline leukaemia, bovine leukaemia, and equine infectious anaemia, all of which share immunological and pathological characteristics with

AIDS in man; second, certain animal retroviruses exhibit an affinity for lymphocytes, which is a characteristic expected of the etiological agent of AIDS.

In the 20 May 1983 issue of *Science*, workers in the USA at the Harvard School of Public Health, the Centers for Disease Control, and the National Institutes of Health presented serological, virological, and epidemiological evidence of an association of human T-cell leukaemia virus-I (HTLV-I) with AIDS. HTLV-I had previously been identified as the cause of adult T-cell leukaemia, neoplastic disease common in southern Japan but rare in the United States. It was believed that positive antibody findings with HTLV-I reflected cross-reactions with the possible causative agent. In the same issue of *Science*, workers at the Pasteur Institute in Paris reported the isolation of a new retrovirus, from a patient with lymphadenopathy syndrome (LAS), and therefore named by them lymphadenopathy-associated virus (LAV). Antibodies to LAV were subsequently found to be present in a significantly higher proportion of LAS and AIDS patients than in controls. These serological findings, together with further isolations of LAV from groups at risk for AIDS, and further characterization of the virus, including its tropism for lymphocytes of the T-4 subset and its cytopathic effect on them, were presented by the Pasteur Institute workers at scientific meetings in 1983 and 1984. In the 7 April 1984 issue of *Lancet*, the Pasteur Institute reported that a virus, possibly identical to LAV, was isolated from two siblings with haemophilia B, one of whom had AIDS-like syndrome.

In April 1984, a team of researchers from the National Cancer Institute, USA, and co-workers described multiple isolations of a retrovirus, termed by them human T-lymphotrophic retrovirus-III (HTLV-III), from AIDS patients. These studies are reported in the 4 May 1984 issue of *Science*. The key to these findings was the development of a continuous T-cell culture system which facilitates virus isolation from patients and permits high-level production of virus.

Rates of antibodies to HTLV-III in AIDS patients and population groups at high risk of AIDS were very similar to those found by the Pasteur Institute with LAV. The similarity of these findings and other characteristics suggest that HTLV-III and LAV are the same viruses, but they have not yet been directly compared in the required biochemical and immunological tests. The determination that the viruses are similar would further support their causative role in AIDS.

Further study is required before these isolates can be confirmed as the etiological agents of AIDS, but the present evidence is highly promising and suggests that better diagnostic and screening tests for AIDS will be developed in the near future, followed by specific prevention and control measures.